Claims 1 and 66 are now directed to a "full-length nucleotide" (see, for example, page 3, lines 3-9 of the specification) and Claims 1, 15 and 66 are now directed to a "crystalline S-layer protein" (see, for example, page 24, lines 15-18).

All of the claims find support in the specification as filed and no new matter has been added. Accordingly, consideration and entry of the amended claims is requested.

I. Response to Rejection of Claims 1, 3, 15-17, 19, 20, 46, 47 and 58-63 under 35 U.S.C. §102(b)/103(a)

Claims 1, 3, 15-17, 19, 20, 46 and 47, and now 58-63 are rejected under 35 U.S.C. §02(b) as being anticipated by Kuen et al (Gene, 1994) and/or obvious in view of Kuen and Deblaere.

A. Response to 102(b) rejection

The Examiner alleges that in view of Kuen disclosing

a) cloning and expression of a S-layer protein in a prokaryotic cell system;

b) the nucleic acid sequence of the S-layer protein including the signal sequence of the sbs gene (abstract; p. 116, col. 1);

c) cells for transformation and

d) a vector (p. 116, Experimental and Discussion),

Kuen anticipates the claimed invention.

Applicants traverse the rejection of the claims for the following reasons.

As explained to the Examiner in the teleconference of December 20, 2001, Applicants respectfully resubmit that:

Kuen did not clone or express a full length protein as originally obtained from a full length clone of the gene;

A full-length clone of Kuen was not expr ssed in *E. coli* or any other prokaryotic cell for that matter. Only "The 3'-end was cloned and expressed in Escherichia coli, whereas the 5'-region was amplified from the genome of Bs PV72 by the polymerase chain reaction using two overlapping fragments." Thus, only an incomplete fragment of the S-layer protein was ever produced and expressed in a prokaryotic system;

Kuen cloned the sbsA gene in a pUC18 vector. The subcloned gene would not have been "in frame" but would have resulted in expression of an "out of frame" protein;

Kuen specifically teaches away from using an *E. coli* host cell in which to express a complete S-layer gene since the protein would be unstable within such a host cell or could possibly be toxic to the cell itself.

The surprising and unexpected results of the instant invention are that full-length, crystalline S-layer proteins can actually be formed within the cytoplasm of a gram-negative cell system. Until now, crystalline S-layer proteins have generally been localized to the cell surface of gram-positive organisms.

In view of the foregoing comments and discussion, Applicants submit that the instant claimed invention is novel, and that withdrawal of the anticipation rejection is deemed proper.

B. Response to 103(a) rejection

Even assuming, *arguendo*, that Deblaere as a secondary reference could be combined with Kuen for teaching full-length proteins, Applicants submit that Deblaere does not teach or suggest that full-length crystalline S-layer proteins could be expressed by gram-negative prokaryotic cells much less that the protein would be localized intracellulary within the cytoplasm. Accordingly, Deblaere does not rectify the deficiencies of Kuen.

For all of the above cited reasons, the instant claimed invention is nonobvious over Kuen alone or in combination with Deblaere, and withdrawal of the rejection is deemed proper.

CONCLUSION

In view of the amended claims, the foregoing arguments, and the teleconference with the Examiner on December 20, 2001, Applicants submit that the Examiner's rejections are met and overcome. The claims are now in condition for allowance, and Applicants request that the Examiner allow the application to pass to issuance.

If for any reason the Examiner determines that the application is not now in condition for allowance, it is respectfully requested that the Examiner contact, by telephone, Applicant's undersigned attorney at the indicated telephone number to arrange for a telephone interview to expedite the disposition of this application.

In the event this paper is not being timely filed, the applicant respectfully petitions for an appropriate extension of time. Any fees for such an extension together with any additional fees may be charged to Counsel's Deposit Account 1-2300.

Respectfully submitted,

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LAB/ccd

1. (Twice Amended) A process for production of a [complete] crystalline S-layer protein comprising

(a) transforming a gram-negative prokaryotic host cell with a full-length nucleic acid encoding an S-layer protein selected from the group consisting of (i) a nucleic acid comprising a nucleotide sequence from position 1 to 3684 of SEQ ID NO.1,

(ii) a nucleic acid comprising a nucleotide sequence corresponding to the nucleic acid of (i) within the scope of the degeneracy of the genetic code, and

(iii) a nucleic acid comprising a nucleotide sequence which hybridizes with at least one of the nucleic acids of (i) or (ii) under stringent conditions;

(b) culturing the host cell under conditions which induce expression of the nucleic acid and production of the corresponding protein, and

(c) isolating the protein from the host cell.

15. (Twice Amended) A nucleic acid encoding a full-length, crystalline recombinant S-layer protein selected from the group consisting of

(i) a nucleic acid comprising a nucleotide sequence from position 1 to 3684 of SEQ ID NO. 1,

(ii) a nucleic acid comprising a nucleotide sequence corresponding to the nucleic acid of (i) within the scope of the degeneracy of the genetic code, and

(iii) a nucleic acid comprising a nucleotide sequence which hybridizes with at least one of the nucleic acids from (i) or (ii) under stringent conditions, wherein the nucleic acid contains at least one peptide or polypeptide-coding insertion within the region encoding the S-layer protein.

66. (Twice Amended) A process for production of [an] a crystalline S-layer protein comprising

a) transforming a gram-negative prokaryotic host cell with a full-length nucleic acid encoding an S-layer protein which comprises at least one insertion encoding peptide or polypeptide sequences and selected from the group consisting of

(i) a nucleic acid comprising a nucleotide sequence from position 1 to 3684 of SEQ ID NO.1,

(ii) a nucleic acid comprising a nucleotide sequence corresponding to the nucleic acid of (i) within the scope of the degeneracy of the genetic code, and

(iii) a nucleic acid comprising a nucleotide sequence which hybridizes with at least one of the nucleic acids of (i) or (ii) under stringent conditions;

(b) culturing the host cell under conditions which induce expression of the nucleic acid and production of the corresponding protein, and

(c) isolating the protein from the host cell.